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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,324	07/13/2001	Shizuo Akira	31671-173143	2302

26694 7590 07/29/2003

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EXAMINER

QIAN, CELINE X

ART UNIT	PAPER NUMBER
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1636

12

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/889,324

Applicant(s)

AKIRA ET AL.

Examiner

Celine X Qian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 May 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-51 is/are pending in the application.
- 4a) Of the above claim(s) 8,9 and 12-51 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7,10 and 11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Claims 1-51 are pending in the application. Claims 8, 9, 12-51 are withdrawn from consideration for being directed to non-elected subject matter.

This Office Action is in response to the Amendment filed on 5/14/03.

Response to Amendment

The rejection of claims 1-7, 10 and 11 under 35 U.S.C. 112 2nd paragraph has been withdrawn in light of Applicants' amendment of the claims.

The rejection of claims 1, 3-6, 10 and 11 under 35 U.S.C. 102 (a) has been withdrawn in light of Applicants' submission of certified translation of priority documents.

The rejection of claims 1, 3-5, 10 and 11 under 35 U.S.C. 102 (b) has been withdrawn in light of Applicants' amendment of the claims.

The rejection of claims 1-7, 10 and 11 under 35 U.S.C. 112 1st paragraph (written description and enablement) is maintained for reasons set forth of the record mailed on 10/29/02 and further discussed below.

Response to Arguments

In response to the written description rejection, Applicants argue that ES cell in species other than mouse is available at the time of invention. Applicants argue that teaching from cited references Bradley et al., Campell and Wilmut and Mullins et al. all indicate that ES cell in other species is available at the time of filing. Therefore, Applicants conclude that a person skilled in the art would be able to carry out the invention without undue experimentation.

This argument has been fully considered but deemed unpersuasive. First, it appears that the arguments presented are directed to the enablement rejection rather than the written

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description rejection. The reason for the written description rejection is discussed in detail in the office action mailed on 10/29/02 (see page 3). Briefly, the specification describes only one species of the animal with specific gene knockouts that is unresponsive to bacterial cell components. With limited information disclosed in the specification, an artisan would have not been able to predict whether mutation or deletion of the same gene(s) in other non-human animal would result in the same phenotype compared to the disclosed knockout mice. In addition, the specification does not describe any mice with other genetic background that is unresponsive to bacterial cell components. As such, the structural and functional relationship between the genetic background and the phenotype of the non-human animal is missing. The specification neither describes a representative number of bacterial cell component unresponsive non-human animals by their complete structure nor other relevant characteristics. Therefore, the written description requirement is not met.

Second, the Examiner does not agree with Applicants' assertion that ES cell is available in species other than mouse at the time of filing. The paragraph cited from Bradley et al. by Applicants clearly support the notion that ES cell has not been isolated from other species. Bradley states that although there are reports about isolating ES cells from farm animals, they have not demonstrate that the isolated cells can proliferate and differentiate in an embryo *in vivo* that contributes to somatic tissue or germ cells. The ability of ES cells to proliferate and differentiate into somatic tissue or germ cells *in vivo* is the unique property of a true ES cell. Without such characteristic, the cell would not be an ES cell. The success of the genetic modification of mouse genome by homologous recombination in ES cells relies on the ability of modified ES cells to proliferate and differentiate in an embryo so that a mouse carrying such

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modification is generated. Therefore, the claimed invention is not enabled because true ES cells in species other than mouse is not available at the time of filing.

Applicants further cited Campell and Wilmut to support the notion that ES cells are available in other species and thus animal models can be produced. However, the cited paragraph clearly states "In species other than mouse the isolation of ES cells has proven more difficult...as yet there are no reports of any cell lines which contribute to the germ line in any species other than mouse." As discussed in the previous paragraph, without the ability of differentiate into any type of tissue including germ line, a cell may be ES-like, but it is not a true ES cell. The specification does not teach how to use such a cell to make a non-human animal with claimed phenotype. Therefore, the claimed invention is not enabled.

Applicants also cited Mullins et al. and conclude that germ transmission is not a necessary requirement in producing model murine and major efforts have been made to generate ad use ES cells from nonmurine species. Applicants clearly misconstrue the meaning of the quoted paragraph. Mullins et al. states "Despite the lack of germline transmission to date, major efforts continue to be directed towards generation and use of ES cells from nonmurine species...and the availability of such cells is likely to accelerate both the use of such species and precision with which genetic changes an be introduced." Such statement does not suggest anything even close to the notion that germline transmission is not required in producing transgenic mouse. On the contrary, Mullins et al. state "Although to date chimeric animals have been generated from several species including pig, in no species other than mouse has germline transmission of an ES cell been successfully demonstrated. This remains a major goal for the future and may well require the use of novel strategies which depart widely from the traditional

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methods used in mouse.”(see page 1558, 2nd col., last two sentences) Mullins et al. also state “if isolation of suitable ES cells and application of homologous recombination becomes a reality in the pig, it may be possible to knockout the antigenic determinants to which antispecies antibodies bind, as a further strategy for HAR.”(see page 1559, 2nd col., last sentence) Such statements clearly indicate that germline transmission is required in generating targeted gene manipulation through homologous recombination in ES cells. In addition, even there are reports about generating chimeric pig, Mullins et al. clearly do not consider the isolation of suitable ES cells in pig a reality. Therefore, all the cited references support the fact that no ES cells other than mouse is available at the time of filing.

Upon reviewing the amendment filed on 5/14/03, it appears that Applicants did not address the enablement rejection (other than the arguments discussed above). Therefore, the rejection is maintained for same reasons set forth of the record mailed on 10/29/02.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

This application contains claims 8, 9, 12-51 drawn to an invention nonelected with traverse in Paper No. 7. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO**

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
July 25, 2003



JAMES KETTER
PRIMARY EXAMINER